WSA

IARC - Multicenter Case-Control Study of ETS and Lung Cancer:

An Analysis:

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Source: https://www.industrydocuments.ucsf.edu/docs/sggk0000

Study characteristics:

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- 12 centers; 7 european countries
- 650 cases; 1542 controls
- Enrollment between 1988 and 1994
- Common questionnaire, (bar translation differences)
  - **Estimates of ETS exposure; Occupational Exposure; Urban/Rural living; Education* and Diet***
- Some inter-center & intra-country differences: Response rate / selection of controls / age groups / Diagnostic criteria

*Data on education and diet not available for all centers.

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Results:

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Reported source of ETS exposure:	No exposed (Cases/ controls)	OR (95% CI)	Inter-center range:	Intra-country (G1/G2/G3) (I1/I2/I3)
Childhood:	389/1021	**0.78*** (0.64-0.96)	0.45-2.09	**(0.60/0.82/0.55)** (0.62/2.09/0.60)
Spousal:	344/700	**1.16(n.s.)** (0.93-1.44)	(<0.7 - >1.5)	-
Workplace:	374/855	**1.17(n.s)** (0.94-1.51)	(8 cntrs >1.0)	-
Workplace or spousal:	527/1201	**1.14(n.s)** (0.88-1.47)	0.72-2.29	**(0.88/1.22/2.01)** (0.73/1.12/1.39)
Overall vehicles:	125/310	**1.14(n.s)** (0.88-1.48)	0 – 2.85	-
Overall public places:	174/454	**1.03(n.s)** (0.82-1.29)	0.24-2.32	-

*** = Statistically significant. n.s = not statistically significant**

G1/G2/G3 & I1/I2/I3 = ORs for German centers 1, 2 & 3; & Italian centers 1, 2 and 3

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Six

Four largest ETS studies: (Spousal)

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Study/Year	Number of cases	OR (95% CI)*
IARC 1998	650	**1.16** (0.93-1.44)
Fontham 1994	651	**1.29** (1.04-1.60)
Brownson 1992	431	**1.00** (0.80-1.20)
Wu-Williams 1990	417	**0.70** (0.60-0.90)
Gao 1987	246	**1.19**** (0.82-1.73)
Sun 1996	230	**1.16** (0.8-1.69)

***Factors adjusted for, and method of adjustment vary by study**

**** Gao 1987 only unadjusted data available**

Combined meta-analysis (fixed effects) = 1.03 (0.93-1.13)

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Potential sources of Bias

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- Selection bias / recall bias
- Diagnosis:
  - Total (Sp or wkplace): OR=1.14 (0.88-1.47)
  - Histologically confirmed: OR=1.11 (0.86-1.43)
- Misclassification:
- Confounding:
  - Accuracy of measurement
  - Residual confounding
- Analysis (conditional versus unconditional)
- **COMBINED EFFECT OF ALL BIASES**

Source: https://www.industrydocuments.ucsf.edu/docs/sggk0000

Estimated effects of some sources of bias:

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Source of potential bias:	Reported Spousal	Workplace	Spousal or Workplace:
Unadjusted OR:	**1.16**	**1.17**	**1.14**
Misclassification bias:	-0.03	-0.03	-0.03
Histological confirmation:	-0.03	-0.03	-0.03
Unconditional analysis:	-0.01	-0.07	-0.03
Confounding:	-0.01	_	-0.01
Estimated overall adjusted OR:	**1.08**	**1.04**	**1.04**

Correction E 50% 89% 91%

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IARC on consistency.

"In the light of the inconsistent findings of other studies, our results on childhood ETS exposure can be plausibly interpreted as sampling fluctuation around a relative risk of 1 (no effect) and do not allow us to conclude that ETS exposure during childhood is protective against lung cancer"

Source: https://www.industrydocuments.ucsf.edu/docs/sggk0000

"Certainty" of the data

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IARC SUMMARY:

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- Large, well conducted study
- No statistically significant overall increase observed for any of the sources of ETS reported.
- Additional adjustments, not made by the study investigators, would have reduced the observed OR even further
- Parallel investigations into potential mechanisms also failed to provide supportive evidence.

Source: https://www.industrydocuments.ucsf.edu/docs/sggk0000

SUMMARY:

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- IARC has performed one of the largest, best conducted studies on ETS exposure and lung cancer risk in non-smokers
- They found no statistically significant increase in overall risk for any of the sources of exposure investigated
- They argue that "consistency" with other epidemiological studies gives them confidence that there is an increase in risk

However:

- They chose not to make several adjustments, (for which they had considerable data), which would have decreased the OR towards the null value, (i.e. no effect)
- Their own investigations into potential mechanisms have failed to provide any supportive evidence

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Workplace: Fontham cf IARC

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	Unadjusted (crude) OR (95% CI)	Adjusted OR (95% CI)
IARC – Spousal	**1.06** (0.87-1.30)	**1.16** (0.93-1.44)
IARC – Workplace	**1.09** (?)	**1.17** (0.94-1.45)
Fontham – Spousal	**1.26** (1.04-1.54)	**1.29** (1.04-1.60)
Fontham – Workplace	**1.12** (0.91-1.36)	**1.39** (1.11-1.74)

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